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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/970,045	11/13/1997	EUGEN KOREN	20487/113	2118

7590 07/06/2005

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EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 07/06/2005

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 08/970,045

Filing Date: November 13, 1997

Appellant(s): KOREN ET AL.

Steven L. Highlander

For Appellant

S.O.O.

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12-23-03.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The Appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

The final rejection was mailed on 10-2-02. The first after final amendment submitted on 1-2-03 was not entered. Subsequently, the application was abandoned and then revived by Appellant. The second after final amendment was filed concordantly with an Appeal Brief on 7-18-03, this proposed amendment was not entered and the Brief as relying upon it deemed defective. A third after final amendment filed with the corrected Appeal Brief of 12-23-03 and was entered into the record.

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(5) Summary of Invention

The summary of invention contained in the brief is deficient because it is a mere reiteration of the claims and points to pages that do not describe the claimed invention. The claimed invention of claims 12 and 13 directed to the use of three antibodies for a ratio finds sole support at Example 10, pages 66-68. The antibodies (AibD5 and CdB5) used in this example have the claimed and recited properties of binding different stable, conformation independent epitopes that are uninfluenced by the lipid content of the lipoprotein protein component of the lipoprotein or lipid associated with the specific lipoprotein. The invention of claim 40 finds sole support at Example 11, pages 68-71 of the specification. It is noted for the benefit of the board that it is well established in the art that lipoproteins (LDL, HDL, VLDL) comprise both a protein component also called apolipoprotein and a lipid component. A lipoprotein may have multiple different and sometimes overlapping apolipoprotein components with other lipoproteins. See art of record.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows:

Claims 12 and 13 also stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as set forth in the Final Rejection mailed 10-2-02.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 12-13 and 40 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Appellants have amended the base claim 12, to recite, "...subtracting from the total apolipoprotein bound.. apolipoproteins". However, this recitation apparently fails to have written description support in the specification as filed. This issue is best resolved by

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Appellants' pointing to the specification by page and line number were support for the amendment can be found.

Claims 12, 13 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention.

As to claims 12 and 13, as set forth in the Office action of 6-27-00 it is unclear as to which first of second antibody binds which apolipoprotein, the claim indicates that there are at least two. It is unclear how the apolipoproteins are distinguished each from the other because the mixed sample contains at least two apolipoproteins which each have antibodies bound and a third antibody immobilized that binds either of the different apolipoproteins. How is separate quantitation achieved? How are two separate apolipoproteins detected? The method steps are missing unknown undefined critical elements which are required to achieve quantitation of two separate apolipoproteins. The assay as claimed merely mixes together the sample, the first and second monoclonal antibodies and the third immobilized monoclonal antibody. No separation or other step is performed. Thus, the mixture as recited in the claims have complexes of mixtures of antibodies from which in some unknown manner some determination is made to achieve the goal of the preamble "a relative concentration of two different apolipoproteins". As further set forth in the Office Action of 10-2-02, the recitation of "...subtracting the

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total/ apolipoprotein bound by the first and second antibodies.." has no antecedent basis in the claims.

As to claim 40, as set forth in the Office Action of 6-27-00, the claim in line 11, states "... separating the complexed antibody-lipoprotein particles from the biological sample.." is renders the claims unclear since it is unclear which complexes are separated and how. It appears that the lipoproteins complexed with the A social antibody separated and thus it is unclear how determining the amount of ApoCIII associated with Apo B is achieved when the pan B antibody is added to the biological sample and not the mixture of the sample and anti-Apo-c antibody. The claims do not make it clear how both antibodies make it into the same sample. The same concern is apparent for the recitation of "... contacting the anti-Apo A-I antibody with the biological sample" in the latter half of the assay for HDL. It is the latter part of the rejection with respect to determination of HDL that is under appeal.

(11) Response to Argument

With respect to the rejection of claims 12 and 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, this rejection was not addressed in the Appeal Brief and therefore, the correctness of the rejection is therefore conceded by Appellant. As previously set forth in the advisory actions, Example 10 is directed to relative staining intensities (i.e. a ratio), no specific concentration was measured by means of subtraction and as such the method step is not supported by argued

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Example 10. The Example is limited to staining intensities of two individual dipsticks the latter of which is not quantitative and relative staining intensities were visually compared. Page 68 indicates that the staining intensities can be compared to known control values to ascertain the concentration. Therefore, the amount of staining intensity is determined, not the concentration. The specification indicates that for the second apolipoprotein (i.e. A-II) "The latter dipstick captures only LPA-I:A-II *subfraction* [emphasis added] which represents approximately 60% of all Apo-I-containing particles..". Thus, while the first dipstick is able to detect total A-I, the second dipstick only detects AII in association with A-I in the same particle because the detecting antibody was in fact anti-A-I. Therefore, this assay does not detect the total amount of A-II. Example 10 does not support subtraction to find the amount of the individual apolipoproteins. Example 10 does not subtract anything, but merely visually compares stained dipsticks to controls. There is no implicit or explicit subtraction step. Visual comparison of relative staining intensities does not support subtracting one amount from another to obtain a third value to use in a ratio.

With respect to the rejection of claims 12 and 13 under 35 U.S.C. 112, second paragraph Appellant's arguments are again not persuasive. Appellant improperly attempts to rely upon allowed claim 1 for interpretation of the vagueness and metes and bounds of claim 12. The interpretation of the metes and bounds of claims 12 and 13 must stand in view of the language of those claims. Appellant cannot rely upon method steps in the

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allowed claims to interpret the metes and bound of the appealed claims, such is a tacit admission that extraneous material and steps are needed to interpret the metes and bounds of assay language of claims 12 and 13. Appellant newly argues that the preamble for determining the relative concentrations of two apolipoproteins and there is nothing inconsistent about the method steps and the preamble. This is simply not so. A concentration is an amount per unit. The claims merely detect amount. This is a basis for inconsistency. Appellant argues determination of step (2) as numbered in the brief yields the concentration. This interpretation is not what the claim states. The claim states determination of the amount. Amount is not equivalent to concentration. Further, the claim states determination of the amount of apolipoprotein bound by the first and second monoclonal antibodies. How is this done? The assay forms an admixture that contains, the sample and three antibodies. None of the antibodies are detectably labeled and all in the same pot. Therefore, the admixture comprising the sample contains unbound and bound antibodies. How is then one to determine that bound? This issue is not resolved. There are apparently critical steps missing. Appellant points to the specification Example 10, page 66, line 31 to page 68, line 11 for support for subtracting is the same as determining the difference between. This is not persuasive, page 68 determines not the ratio of two different apolipoproteins but total A-I relative to the A-I present in A-II containing lipoprotein particles. This is a completely different concept. There is no step of determining the difference between the two. The total A-II *per se* is never

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quantitated. Total A-I plus A-II is never quantitated. This subtraction method step does not find support in the Example. It cannot, because total A-II is never quantitated in this Example. A ratio in mathematical terms represents a proportion or percentage and not subtraction. The ratio of the Example 10 is A-I alone to A-I/A-II containing lipoproteins. Nothing has been subtracted from anything else in this example. Appellant argues total of Apo1 plus Apo2 is determined. Again, how? Argued step 5 does not yield concentration of anything only an alleged amount. All three antibodies are in a mixture and it is not apparent how any amount or concentration of any apolipoprotein is determined. Amount is not equivalent to concentration which is an amount per unit (volume, weight etc). Appellant argues that the values are relative since they are determined by reference to each other. This is not persuasive, the same antibody is not used for detection and therefore they are not determined relative to each other. This claim merely provides for a mixture of three antibodies with the sample and somehow an amount is determined. As previously set forth, there is missing critical information on how to do this and subtraction is not supported in Example 10.

With respect to the rejection of claim 40 under 35 U.S.C. 112, second paragraph Appellant's arguments are not persuasive. In the latter half of the claim, step (b) HDL is determined. Appellant amended the claim however, it was still indefinite because the step of "separating the complexed anti-Apo-II antibody-ApoCIII containing lipoprotein particles from the biological sample" references the inappropriate procedure in step (b)

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does not achieve the goal. It is noted that this procedure alternatively references the same complex in step a. Therefore, the procedure in step (b) does not quantitate HDL. The way this claim step is written it improperly references multiple different parts of the claim. The complexed anti-Apo-CIII antibody-ApoCIII containing lipoprotein is set forth in step (a) and step (b). Even if this was not an antecedent basis problem, then it is still unclear how the amount of Apo-CIII present in HDL in the anti-Apo-CIII antibody-Apo AI complexed material is determined when the complexed anti-Apo-I antibody-ApoC-III containing lipoprotein particles from the biological sample. As previously set forth, the complex that should be separated is the anti-Apo-CIII anti Apo-I complexed material in order to determine the amount of ApoC-III present in the anti-ApoCIII anti-Apo AI complexed material in the sample as set forth in step (b) of the method claim. Appellants continue to argue that step (b) yields a total of ApoCIII bound in HDL. This is simply not so because the ApoCIII lipoprotein complex is separated out. The method steps are not limited in this claim to any specific order. The separation of the ApoCIII containing lipoprotein means that anti-Apo-I antibody-ApoC-III containing lipoprotein particles can not be determined since they cannot be formed because all Apo CIII lipoprotein complexes are "separated" or removed. Appellant asserts that while they did not list every single step which might be encompassed within the claimed method, the claims only define that which is Appellant's invention and not that which is known and routine. This is not persuasive, the method steps must define the critical steps of the invention to achieve

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the goal of the preamble. These methods do not define steps that allow the skilled artisan to envision how the assay works to achieve the goals of the preamble. The omitted steps are critical to the functioning of the assay. While Appellant does not have to provide every immunoassay step, the steps set forth in the assay claims must function to perform the assay in clear and unambiguous manner to circumscribe the invention. These claims do not.

For the above reasons, it is believed that the rejections should be sustained.

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Respectfully submitted,

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June 27, 2005

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